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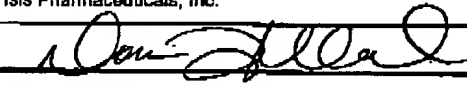
PTO/SB/21 (09-04)

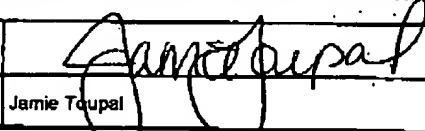
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<b>TRANSMITTAL FORM</b>  (to be used for all correspondence after initial filing)	Application Number	09/920,033	
	Filing Date	08/01/2001	
	First Named Inventor	Rosanne M. Crooke	
	Art Unit	1635	
	Examiner Name	Janet Epps-Ford	
Total Number of Pages in This Submission	3	Attorney Docket Number	ISPH-0592

ENCLOSURES (Check all that apply)		
<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement  <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Reply to Missing Parts/Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation <input type="checkbox"/> Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD	<input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): Letter to Examiner
Remarks		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT			
Firm Name	Isis Pharmaceuticals, Inc.		
Signature			
Printed name	Donna T. Ward, Ph.D.		
Date	09/01/2005	Reg. No.	48,271

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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Crooke et al.

Application No: 09/920,033

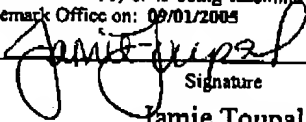
Group No: 1635

Filed: August 1, 2001

Examiner: Epps-Ford, Janet

Confirmation No.: 5785

Title: ANTISENSE MODULATION OF APOLIPOPROTEIN B-EXPRESSION

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LETTER

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Examiner Epps-Ford:

This letter is further to the reply filed on June 15, 2005. No fees are believed to be due in this matter. This letter is prompted by a routine review of the application prior to its allowance. On October 31, 2002, attorney for Applicants filed a response to a restriction requirement. In that response, Attorney Licata stated that "Applicants respectfully disagree that the sequences set forth by the Examiner are distinct as being novel and unobvious over each other, as required by MPEP § 802.01." Applicants would like to clearly state that they vehemently disagree with Attorney Licata's statement. The data presented in the patent application establishes that different targeting sequences can possess very different degrees of properties. This data clearly teaches that sequences that

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target the same gene can be patentably distinct from each other. Of course, the Examiner did not adopt this clearly erroneous position. The Applicants of the application and their assignee were not aware of and/or did not appreciate the statement at the time this paper was filed. This letter is filed solely to clarify the record and Applicants' opinions regarding the patentable distinctness of the sequences disclosed and claimed in this application. It is possible that Attorney Licata has made similar arguments in other applications prosecuted on behalf of the present Applicants and assignee. Again, the Applicants and their assignee believe that such a statement cannot be made in most applications relating to antisense compounds directed to any particular target. It is explicitly requested that the Patent Office deem this statement as satisfying its duty under 37 CFR 1.56 to disclose such inconsistent statements, if any such statements exist.

#### Conclusion

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at 760-603-2528.

Respectfully submitted,

By 

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Dated: 9/1/05